1. PURPOSE

1.1. This document establishes the definitions followed by the human research protection program at the University of Miami.

2. REVISIONS FROM PREVIOUS VERSION

2.1. Addition of definition of Central IRB (3.2)
2.2. Addition of definition of Medical Case Reports (3.19)
2.3. Revised definition for Serious Non-Compliance (3.30)
2.4. Addition of definition of Wards (3.34)
2.5. Addition of definition of Withdrawal (3.35)
2.6. Consolidation of definitions across the HRSO Reconciliation to Huron HRPP Toolkit 4.5, dated 12/10/2021

3. GUIDING PRINCIPLES

3.1. Allegation of Non-Compliance: An unproved assertion of Non-Compliance.
3.2. Assurance of Compliance (Human Subjects) or Federalwide Assurance: An assurance is a written commitment to protect human research subjects and comply with the requirements of the Common Rule.
3.3. Authorization Agreement: Also called a Reliance Agreement, is the agreement that documents respective authorities, roles, responsibilities, and communication between an institution/organization providing the ethical review and a participating institution relying on the ethical review.
3.4. Central IRB: The IRB of record that provides the ethical review for all sites participating in more multisite studies. The sites are usually in a consortium, a network or a particular program.
3.5. Certificate of Confidentiality: A Certificate of Confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), 42 U.S.C. 241(d) amended by Section 2012 of the 21st Century Cures Act, Public Law 114-255, to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not disclose information in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.
3.6. Certification: The official notification by the institution to the supporting Federal department or agency component that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.
3.7. Clinical Trial: A prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective.
3.8. Collaborative Study: A study in which two or more institutions coordinate, with each institution completing a portion of the research activities outlined in a specific protocol.
3.9. Conflicting Interest: An individual involved in research review is automatically considered to have a conflicting interest when the individual or the individual's

spouse, domestic partner, children, and dependents have any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual's immediate family:

3.9.1. Involvement in the design, conduct, or reporting of the research.

3.9.2. Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.

3.9.3. Compensation of any amount in the past year or of any amount expected in the next year, excluding compensation for costs directly related to conducting research.

3.9.4. Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.

3.9.5. Board or executive relationship, regardless of compensation.

3.9.6. Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.

3.9.7. Any other reason for which the individual believes that he or she cannot be independent.

3.10. Continuing Non-Compliance: A pattern of Non-Compliance that suggests the likelihood that, without intervention, instances of Non-Compliance will recur, a repeated unwillingness to comply, or a persistent lack of knowledge of how to comply.

3.11. Designated Reviewer: The IRB chair or an Experienced IRB Member designated by the IRB chair to conduct Non-Committee Reviews.

3.12. DHHS: Department of Health and Human Services.

3.13. Data Safety and Monitoring Committee/Data Safety and Monitoring Board (DSMC/DSMB): A committee of clinical research experts, such as physicians and statisticians, and patient advocates who monitor the progress of a clinical trial and review safety and effectiveness data while the trial is ongoing. This committee is independent of the people, organizations, and institutions conducting the clinical trial. This committee can recommend that a trial be stopped early because of concerns about participant safety or because the main research question has been answered.

3.14. Emergency Use: The use of an investigational a drug, biologic, or medical device on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)).

3.15. Expanded access: The FDA has several specific mechanisms and regulations that allow use of an investigational item outside of a formal clinical trial. This is called expanded access.

3.16. Experienced IRB Member: An IRB member is considered experienced if the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.

3.17. Expiration Date: The first date that the protocol is no longer approved. The date after the end date of the approval period.

3.18. FDA: Food and Drug Administration

3.19. Finding of Non-Compliance: Non-Compliance in fact
3.20. HRPP: Human Research Protection Program.
3.21. Human Research: Any activity that either:[1]
  3.21.1. Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or
  3.21.2. Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.
3.22. Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Private Information and Identifiable Information. For the purpose of this definition:
  3.22.1. Intervention: Physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
  3.22.2. Interaction: Communication or interpersonal contact between investigator and subject.
  3.22.3. Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
  3.22.4. Identifiable Information: Information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).
3.23. Human Subject as Defined by FDA: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used.
3.24. Immediate Family: Spouse, domestic partner; and dependent children.
3.25. Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject to affirm the completeness of the consent process.
3.26. Independent Monitor: A person not involved with the research assigned by the IRB or Institutional Official or designee to verify that (a) the rights and well-being of human subjects are protected; (b) the reported trial data are accurate, complete, and verifiable from source documents; and (c) the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

[1] The terms "Human Subject Research," "Research Involving Human Subjects," "Clinical Research," "Clinical Investigation," "Clinical Study" and similar phrases are considered to be synonyms for the term Human Research.

3.27. Institutional Official: The Vice Provost for Research.

3.28. Institutional Official/ Organizational Official (IO/OO):

3.28.1. Institutional Official (IO): Term utilized by DHHS.

3.28.1.1. The Institutional Official (IO) is the individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the Terms of the Assurance. The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the institution named in the Federalwide Assurance (FWA)[2]. The IO is often the Vice President for Research.

3.28.2. Organizational Official (OO): Term utilized by AAHRPP.

3.28.2.1. An identified, knowledgeable leader of the HRPP who is responsible for the program and has the authority to implement the program. This individual may rely on others for the interpretation of laws, regulations, codes, and guidance and the day-to-day operations of the HRPP, and should have a basic understanding of the relevant laws, codes, regulations and guidance that govern research involving human participants, the responsibilities of an organizational official, and the responsibilities of the IRB or EC and researchers and research staff in protecting research participants. This individual should be directly involved in the allocation of resources to the HRPP. In some circumstances, more than one individual serves in this capacity[3].

3.29. Institutional Profile: A record of information an institution keeps about another collaborating institution/organization for one or more Collaborative Studies or Multi-Site Studies.

3.30. Investigation: A searching inquiry for facts; detailed or careful examination.

3.31. Investigational Device Exemption (IDE): An IDE application is the document submitted to the FDA for permission to conduct a clinical study using a significant risk device that is new or not approved for a given use. When the FDA approves an IDE application, it assigns an IDE number to the specific use of the device.

3.32. Investigational New Drug (IND): An IND application is the document submitted to the FDA for permission to conduct a clinical study using a drug or biologic that is new or not approved for a given dosage, formulation, or indication. When the FDA approves an IND application, it assigns an IND number to the specific use of the item.

3.33. Investigational: This term is used to refer to an item that is not FDA-approved for

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[2] https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2008-september-18-letter-attachment/index.html

[3] AAHRPP Evaluation Instrument (2018-10-15); http://www.aahrpp.org/apply/web-document-library/domain-i-organization

marketing in the United States, or to an item that is being evaluated for a new and not-yet-approved indication, dosage, or formulation.

3.34. Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures(s) involved in the research.

3.34.1. If there is no applicable law addressing this issue, then this individual is recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

3.34.2. See HRP-013 - SOP - LARs, Children, and Guardians for who may serve as a Legally Authorized Representative at this institution.

3.35. Medical Case Report: Medical case reports of 1-3 patients that fit the following criteria do not meet the federal definition of human subject research since the information in the case report is not considered generalizable knowledge. Therefore, clinicians at the University are not required to obtain IRB approval for medical case reports. The review of medical records for publication in such case reports, however, is subject to HIPAA rules and may require authorization from the patient to use the protected health information.

3.35.1. It is a description of medical observations or of an interesting medical condition, innovative treatment, presentation, disease progression or outcome

3.35.2. It relates to three or fewer patients

3.35.3. The patients are those treated by the clinician preparing the report

3.35.4. The report describes observations and is not presented as a systematic investigation designed to contribute to generalizable knowledge

3.35.5. The report contains no data analysis or testing of a hypothesis

3.36. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests[4].

3.36.1. For research involving prisoners Minimal Risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

3.36.2. When following Department of Defense regulations, the definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to include the inherent risks certain categories

[4] The phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" should not be interpreted to include the inherent risks certain categories of subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

of human participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

3.37. Multi-Site Study: A study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol.

3.38. Non-Committee Review: Any of the following:

3.38.1. Determination of whether an activity is Human Research.

3.38.2. Determination of whether Human Research is exempt from regulation.

3.38.3. Reviews of non-exempt research using the expedited procedure.

3.38.4. Determinations of which subjects can continue to be treated when research has lapsed in IRB approval.

3.38.5. Concurrence of IRB Chair or designee for non-emergency individual patient/small group expanded access for an unapproved medical device (commonly known as Compassionate Use) or non-emergency individual patient expanded access IND with request for authorization to use alternative IRB review procedures.

3.39. Non-Compliance: Failure to follow the regulations, or the requirements or determinations of the IRB.

3.39.1. In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) instruction 3216.02, its references, or applicable requirements

3.40. Off-label use: The clinical use of an FDA-approved drug, device or biologic for a purpose or population that has not been approved by the FDA, or in a route or dose that has not been approved by the FDA. Off-label use is not regulated by the IRB or the FDA; it is subject only to any policies and procedures of state law and the clinician's institution.

3.41. Orphan drug: A formal designation by the FDA for drugs primarily intended to treat a rare disease or condition. See the regulations at 21 CFR 316.

3.42. Participating Site (pSite): An institution that participates in a Single IRB (sIRB) Study.

3.43. Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

3.43.1. For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.

3.44. Protocol Exception: a one-time, intentional action or process that departs from the approved protocol. Protocol Exceptions are generally for a single subject (e.g., the subject does not meet eligibility criteria or is allergic to one of the medications provided as supportive care). IRB approval of the Protocol Exception is required prior to implementation by the study team.

3.45. Related to the Research: A financial interest is Related to the Research when the

interest is in:

3.45.1. A sponsor of the research;

3.45.2. A competitor of the sponsor of the research;

3.45.3. A product or service being tested; or

3.45.4. A competitor of the product or service being tested.

3.46. Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

3.46.1. The following activities are not considered Research as Defined by DHHS:

3.46.1.1. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

3.46.1.2. Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.

- Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
- Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
- Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

3.46.1.3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

3.46.1.4. Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.

3.46.1.5. Secondary research involving non-identifiable newborn screening blood spots.

3.46.2.

3.47. Research as Defined by FDA: Any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:

3.47.1. Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;

3.47.2. Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or

effectiveness of a device; OR

3.47.3. Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

3.48. Restricted: Applies to investigators who are delinquent in meeting IRB requirements.

3.49. Serious Non-Compliance: Noncompliance can be defined as failure to comply with regulations, university policies, or the requirements/determinations of the IRB, when, in the judgment of the institution, such failure substantially increases risks to subject welfare/safety, subject rights, or data integrity. Serious non-compliance may also involve compromising the effectiveness of UM's human subject research protection program

3.49.1. For Department of Defense (DOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) Instruction 3216.02 and its references such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.

3.50. Single IRB (sIRB) Study: A study in which two or more institutions (participating sites, or pSites) coordinate to complete the research activities, but all institutions rely on a single institution's/organization's IRB for ethical review. The reviewing IRB may or may not be affiliated with any of the pSites.

3.51. Sponsor: The person, company, organization, or other entity that initiates and takes responsibility for a clinical investigation using an FDA-regulated item. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. The item is administered, dispensed, or used under the immediate direction of another individual.

3.52. Suspension of IRB Approval: An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review.

3.53. Termination of IRB Approval: An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer require continuing review.

3.54. Unanticipated Problem Involving Risks to Subjects or Others: Any information that is (1) unanticipated and (2) indicates that subjects or others are at increased risk of harm.

3.54.1. For Department of Defense (DOD) research the term Unanticipated Problem Involving Risks to Subjects or Others includes any incident, experience, or outcome that meets ALL three of the following conditions:

3.54.1.1. Is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent

document) and the characteristics of the human subject population being studied.

3.54.1.2. Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

3.54.1.3. Suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

3.55. Ward: A child who is placed in the legal custody of the state or other agency, institution or entity, consistent with applicable federal, state or local law.

3.56. Withdrawal of Subjects: Subjects who signed the consent, but later are withdrawn from the study, either before or after receiving a study drug, device or intervention. This includes screen failures if subjects signed consent prior to screening.

4. RESPONSIBILITIES

4.1. Individuals writing SOPs are to indicate terms defined in this SOP with a double-thick underline.

4.2. Individuals using SOPs are to consult this SOP for the definitions of double-thick underlined terms.

5. PROCEDURE

5.1. None

6. MATERIALS

6.1. None

7. REFERENCES

7.1. 45 CFR §46.102.

7.2. 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)

7.3. 45 CFR §46.102

7.4. 45 CFR §46.102

7.5. 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)

7.6. 21 CFR § 50.23; 21 CFR § 50.24; 21 CFR § 56.102(d); 21 CFR § 56.104(c).

7.7. 21 CFR § 812.36; 21 CFR § 812.47.

7.8. 21 CFR § 56.105; 21 CFR § 56.108(c).

7.9. AAHRPP elements I.1.A, I.1.E, I.5.D, I.6.B, I.7.C, I-9, II.1.D, II.2.A, II.2.B, II.2.G, II.2.H, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.A, II.4.A, III.1.B, III.2.D